The Medical Benefits of Beta-1,3D-Glucan

Beta-glucan, a natural chemical extracted from yeast and plant cell walls, is an immune system booster with enormous potential in combatting cancer and AIDS, surgical infection and even the effects of radiation.

by Peter Olson, BA, DipEd

PO Box 393
Byron Bay, NSW 2480, Australia
Fax: +61 (0)2 6684 9143
E-mail: naturehealer@mail.com

[Editor's Note: This article refers to research studies involving animals. We wish to advise readers that we at NEXUS do not condone or support the validity, efficacy or morality of animal experimentation or vivisection.]

Western medicine usually treats patients with antibiotics and patented drugs. Many such drugs have harmful side effects and can weaken our natural immune system. This paper explores the role of Beta-1,3D-Glucan in boosting the immune system as an alternative to conventional medication, and in acting as an adjuvant by enhancing the effectiveness of conventional medication.

Our immune system is our only natural defence against invading disease pathogens, yet it sometimes fails to cope with disease. This is because our immune system is not something that is always activated; rather, it modulates between an active state and an inactive state. When the immune system is fully activated, then virucidal and tumoricidal chemicals made by the body to fight diseases are at high levels. When the immune system is inactive, these same chemicals exist only at very low levels, allowing invading organisms to multiply. Pollution of our environment results in our immune system being increasingly harmed and deactivated; for example, every Western person's body now contains dioxin which can deactivate the immune system.

The immune system always requires stimulation in order to switch from an inactive or normal state to the activated state. A typical stimulus might be the detection by the body of some part of a germ. However, sometimes a disease can progress significantly and the person might get quite sick before the immune system becomes aware of the presence of disease microbes.

There are two types of immune responses: *specific* and *non-specific*. If one is vaccinated against a particular disease, say smallpox, then the subsequent change in the immune system reflects a specific immune response targeted only against smallpox. Alternatively, one can have a non-specific immune response whereby the changes in the immune system are more generalised in nature and not aimed at any single specific disease threat. Such a non-specific immune response is capable of enhancing the body's natural protection against a wide variety of diseases rather than giving protection only against a particular single organism.

In the 1940s, Louis Pillmer, PhD, and his associates discovered that a yeast cell wall extract was capable of producing this kind of non-specific immune response. In the 1960s, Nicholas DiLuzio, PhD, at Tulane University identified the active ingredient of the yeast cell wall extract as beta-1,3D-glucan.

Then in the 1980s, Joyce Czop, PhD, and colleagues from Harvard Medical School went further and described exactly how beta-glucan was able to stimulate the immune system. They found that a key immune cell, called a *macrophage*, contained specific receptor sites which could be activated by the presence of beta-1,3D-glucan. They wrote that "studies indicate that beta-glucans with 1,3 and/or 1,6 linkages are active pharmacologic agents that rapidly confer protection to a normal host against a variety of biologic insults".[1]

So it was that the non-specific immune stimulant beta-1,3D-glucan was discovered. Its protection is brought about through the triggering of biological switches—*receptor sites*—on the macrophage. These receptors are only activated when a particle has exactly the right shape to fit the receptor site—and beta-1,3D-glucan has that particular shape, just as a lock can only be opened by a particular key. After discovering this, Czop et al. wrote

that "the beta-glucan receptors provide a mechanism by which a heightened state of host responsiveness is initiated".[2] The resulting higher levels of cytokines in the blood and enhanced intercellular communication from immune activation messengers mean that the immune system is in a better position to be able to defend the body from invading organisms.

It will be shown that such protection can benefit the body in its defence against viruses, bacteria and cancer, and also to help promote rapid wound healing. A Medline Internet search for beta-glucan will typically find over 6,000 published scientific journal articles on this topic, so this is a well-researched subject.

BETA-GLUCAN AND THE IMMUNE SYSTEM

Beta-1,3D-glucan is a naturally occurring polysaccharide that can be found in a variety of sources in nature, and not only from yeast cell walls. Various kinds of beta-glucan can be extracted from medicinal mushrooms, oats, seaweed and even from inside the cell walls of bacteria. Common starches are types of alpha-glucans. Beta-glucan is merely a common polysaccharide building block found in a number of species of plants, fungi and bacteria. It is the active ingredient in oriental medicinal mushrooms, as used in China and Japan for many centuries.

Glucans are strings of glucose molecules joined together. Different arrangements of the glucose molecules form different glucan structures with different molecular weights and result in varying degrees of immune-enhancing potencies.[3] From all these different types of glucan, it is beta-1,3D-glucan that has been shown to have the best immune-stimulating properties. Some types of beta-glucan are destroyed by stomach acids and so are not orally active, but beta-1,3D-glucan derived from baker's yeast is unaffected by stomach acid and is completely intact when taken into the bloodstream. Although beta-1,3D-glucan is extracted from baker's yeast, it is only a tiny particle from within the yeast cell wall and contains no yeast proteins, so does not adversely affect those who are allergic to yeast.

Beta-1,3D-glucan is a naturally occurring polysaccharide that can be found in a variety of sources in nature, and not only from yeast cell walls.

The fact that the immune system macrophage cell has receptor sites for beta-1,3D-glucan[4] suggests the possibility that the immune system associates detection of beta-1,3D-glucan with the presence of a disease organism. Doctors sometimes test for the presence of beta-glucan in order to detect deep bacterial infection,[5] so scientists also associate the presence of beta-glucan as being indicative of possible bacterial infection. This is because beta-glucan is an inert building block from inside the cell wall of a wide variety of bacteria—just like bricks are used to make a brick wall. So because the immune system associates detection of beta-1,3D-glucan as representing a possible undefined bacterial infection, the immune system macrophage cell will produce a generalised, non-specific immune activation once it detects the presence of beta-1,3D-glucan.[6,7]

In producing such a non-specific immune response, a macrophage needs to go through several stages of activation: resident, primed, activated and, finally, cytotoxic. Normally the macrophage may be "asleep", so to speak, in its resident state, in which case it is smooth, inactive and producing few chemicals such as cytokines. As the macrophage goes through the various stages of activation, its phagocytic ability, cytokine excretion and killing ability increases. Hydrogen peroxide, superoxide and nitric oxide are some of the virucidal and tumoricidal chemicals that are produced once the macrophage has reached the fully activated cytotoxic state.[8] Only then is the fully activated macrophage able to use these chemical weapons to kill bacteria, viruses and cancer cells. A normal person with an inactive immune system may have macrophages that are still "asleep"; these macrophages, not realising that a disease is occurring, fail to respond appropriately and to produce these biological defence chemicals.

Once activated, the macrophage also helps to organise and direct some of the other types of immune system cells. One way it does this is through excreting chemicals called *cytokines* into the blood—chemicals such as interleukins, interferons, tumour necrosis factor, colony stimulating factor and others.[9,10] These chemicals are in turn detected by other types of immune system cells such as B-cells, T-cells and natural killer cells, and leads to the activation of these other types of immune cells around the body. This process is referred to as the *immune cascade*, whereby the triggering into activation of the macrophage and its release of chemical messengers subsequently triggers into activation other types of immune system cells around the body.

Unlike normal medical drugs, chemotherapeutic agents and antibiotics, beta-1,3D-glucan produces a completely natural cell-mediated immune response. The therapeutic effect comes about through the body's own natural defence system and not through consuming some toxic substance that might leave the body weakened as a result. On the contrary, one's natural defences are increased.

ANTI-CANCER EFFECT

The macrophage is one part of the immune system that is capable of killing cancer cells. In addition to organising other immune cells, another function of the macrophage cell is *phagocytosis*: engulfing and then digesting foreign cells and particles.

The macrophage is an extremely large cell compared to all other immune cells, and it has a series of long tentacles resembling those of an octopus. The macrophage tentacles can grab foreign cells, such as cancer cells, and drag them in, engulf them, then digest them using the natural toxic chemicals that the macrophage can produce, such as nitric oxide and hydrogen peroxide.

The ability of the macrophage to digest foreign particles phagocytically varies proportionately with the state of activation of the macrophage. When the macrophage is in its dormant or resting stage, its surface is smooth and its ability to engulf cells is impaired. As the macrophage becomes more activated, its surface becomes progressively more wrinkled, which greatly enhances its phagocytic ability. So macrophage activation increases phagocytosis.

In a study by J. Bogwald et al., the authors showed that glucan-activated macrophages are capable of killing different types of cancer cells such as melanoma and mastocytoma. The authors said that "macrophages stimulated by an insoluble beta-1,3D-glucan from yeast cell walls were able to destroy tumour cells, as

measured by the release of radioactive label from prelabelled 14C-thymidine cells".[11]

Other authors have found similar results. Di Luzio et al. found that glucan was capable of producing a "significant reduction in the growth of mammary carcinoma and melanoma B16", and concluded that "glucan initiates significant antitumor activity".[12] In a separate study, Di Luzio et al. found that glucan produced "inhibition of tumor growth and enhancement of survival in a variety of transplantable tumors".[13]

In Japan, extracts containing various types of beta-glucan have been used successfully to assist in the treatment of cancer patients for the last 20 years.[14]

Additional evidence of the antitumour effects is given by R. Seljelid, who stated that "when water-soluble aminated beta-1,3D-glucan was injected intravenously or intraperitoneally on day seven of tumor growth, the tumors underwent complete regression".[15]

Similar injections of beta-glucan into tumours, performed by Mansell et al., also showed positive results. The authors injected beta-1,3D-glucan directly into patients with a variety of tumours, including breast cancer and melanoma. Although the number of patients was small (nine patients), they found in every case that "the size of the lesion was strikingly reduced in as short a period as five days" and "the amount of glucan injected and the quantity of residual tumor appeared to be related",[16] suggesting a dose-response correlation.

Scientists are well aware that sometimes our immune system simply fails to recognise and hence kill cancer cells, resulting in the uncontrolled growth of the cancer. Researchers at the University of Louisville, USA, showed that beta-1,3D-glucan could help the immune system to target and then kill cancers that otherwise would have gone unrecognised and hence unaffected by the immune system. The authors wrote: "Despite exhibiting membrane-bound C3, breast tumor cell lines were not killed by CR3-bearing natural killer cells. Priming of natural killer cell CR3 with small, soluble yeast beta-glucan polysaccharides enabled CR3-dependent killing of these same C3-bearing tumor cell lines".[17] So beta-1,3D-glucan assists the immune system in recognising cancer cells from normal cells.

Scientists are well aware that sometimes our immune system simply fails to recognise and hence kill cancer cells, resulting in the uncontrolled growth of the cancer.

Beta-glucan exhibits not only a direct anti-tumour effect via macrophage activation and enhanced cancer cell recognition, but also shows a synergistic effect when used in combination with conventional anti-cancer drugs. K. Gomaa et al. state that when used alone, "glucan exhibited a strong inhibition of tumour growth of the allogeneic sarcoma-180". However, they wrote that in testing the synergistic effect of glucan with anti-cancer drugs, "against the hormone-sensitive Noble-Nb-R prostate carcinoma the glucan alone showed a moderate antitumour effect, whereas in combination with diethylstilbestrol an almost complete regression of the tumour could be achieved".[18] This is just one of many examples where glucan has been shown to have a synergistic effect when combined with other medications.

Obviously every large, lethal, solid tumour began life as a single cancer cell. It would seem possible that everyone might develop a single cancer cell somewhere in their body during their lifetime, yet not everyone dies of cancer or even develops a noticeable cancer. It would seem possible that people with an active immune system may have macrophages in an activated state which can easily overcome and phagotise isolated single cancer cells in the body. On the other hand, if the natural defences are weakened through exposure to environmental contaminants and a single cancer cell develops, then that single cancer cell may go unrecognised and unchallenged by the body's weakened natural defences. It would multiply and eventually would become millions of cancer cells and a much bigger problem for the body to deal with.

The concept of an ingredient working synergistically with a drug is called the *adjuvant principle*. The *Merriam-Webster Medical Dictionary* defines *adjuvant* as "assisting in the prevention, amelioration or cure of disease".[19] Not only does beta-glucan have a direct effect as a biological response modifier when used alone, but it frequently demonstrates an adjuvant effect by working synergistically with other drugs.

SYNERGY WITH ANTIBIOTICS

Just as beta-1,3D-glucan works synergistically with anti-cancer drugs, it also works synergistically when used in combination with antibiotics. Doctors from Harvard Medical School conducted randomised, double-blind, phase 1/2 clinical trials of a modified beta-glucan, called PGG-glucan, to test its effectiveness in infection control in high-risk surgical patients. The results of the clinical trials were very clear and statistically significant: beta-glucan greatly reduced the rate of infection in these patients. The Harvard researchers stated: "Patients who received PGG-glucan had significantly fewer infectious complications (3.4 infections per infected patient vs 1.4 infections per infected patient, $p = 0.05$), decreased intravenous antibiotic requirement (10.3 days vs 0.4 days, $p = 0.04$) and shorter intensive care unit length of stay (3.3 days vs 0.1 days, $p = 0.03$)." They concluded that "glucan is safe and appears to be effective in the further reduction of the morbidity and cost of major surgery" and, further, that "there were no adverse drug experiences associated with PGG-glucan".[20]

Another Harvard Medical School study of glucan found similar positive results. The authors found "a dose-response trend with regard to infection incidence" among patients who received glucan—meaning that the higher the dose of glucan, the smaller was the resulting incidence of patient infection.[21]

In 1999, doctors from the University of Washington School of Medicine conducted a multicentre, prospective, randomised, double-blind, placebo-controlled trial of a type of beta-1,3D-glucan on patients scheduled for gastrointestinal operations. Thirty-nine medical centres throughout the United States were involved. All patients received standardised antibiotic

prophylaxis. In the noncolorectal group (391 patients), "glucan administration was associated with a statistically significant relative reduction (39%) in serious infections and death". In malnourished patients having these operations, infections and death were 44% of 70 patients in the placebo group, 24% of 68 patients in the low-dose glucan group, and 17% of 72 patients in the higher-dose glucan group. This represents a 61% reduction in the rate of infection between the controls and the higher-dose glucan group of malnourished surgical patients. That would seem to be a remarkable finding for a long studied, yet little used natural product. The authors predicted that "glucan would become an important product in infectious disease management".[22]

Doctors in Brazil have also conducted double-blind clinical trials which demonstrate the ability of beta-1,3D-glucan to reduce infections in hospital patients and prevent death. The authors wrote that "Pneumonia occurred in 11 of 20 patients in the control group and in two of 21 recipients of glucan ($p < 0.01$)" and that "The mortality rate related to infection was 30.0 per cent in patients in the control group and 4.8 per cent in the group treated with glucan ($p < 0.05$)".[23] It is easy to see that glucan, a natural polysaccharide molecule, saved people's lives during these hospital-based clinical trials by working synergistically with conventional antibiotic medication.

Researchers from Tulane University, USA, conducted randomised, double-blind clinical trials of beta-glucan to assess mortality rates in patients due to infection caused by trauma. Browder et. al. found that "the total mortality rate was significantly less in the glucan group (0% versus 29%)" compared to controls, and that "Glucan therapy significantly decreased septic morbidity 9.5% versus 49%". They stated that these beneficial effects are attributable to enhanced macrophage function produced by glucan.[24] This particular study, demonstrating the effectiveness of beta-glucan at mortality reduction by enhanced infection control, is over 10 years old, yet few if any general practitioners have ever heard of this natural product, beta-1,3D-glucan.

A search of the National Library of Medicine found 31 journal articles discussing the radioprotective effects of beta-1,3D-glucan.

The US Army is amongst those who have reported positive findings on the radioprotective properties of glucan.

DISEASE RECOGNITION

Activated macrophages can aid in the immune system's identification of bacterial or viral invaders. If an activated macrophage encounters a virus and phagocytically digests it, the macrophage will then display part of that virus, called an *antigen*, on the macrophage surface. If an immune system T-cell comes along, it will be able to recognise the antigen being displayed by the macrophage and elicit a specific T-cell response aimed at that particular virus.[25] The T-cell cannot recognise the virus and initiate that response until after the virus is broken down and its viral antigen is displayed on the macrophage surface.

In an animal study, researchers concluded that "glucan is capable of increasing survival, inhibiting hepatic necrosis, and maintaining an activated state of phagocytic activity in mice challenged with mouse hepatitis virus".[26]

RADIOPROTECTIVE EFFECTS

A search of the National Library of Medicine found 31 journal articles discussing the radioprotective effects of beta-1,3D-glucan.

The US Army is amongst those who have reported positive findings on the radioprotective properties of glucan. Some of the effects of nuclear radiation are damage to the bone marrow, colony-forming cells and haematopoietic progenitor cells that manufacture blood cells. Researchers found that glucan exhibited a radioprotective effect because of its ability to stimulate recovery of the bone marrow cells after radiation damage and subsequently the haematopoietic regeneration of new blood cells.[27, 28]

These results have been confirmed by many researchers. For example, M. Hofer et al. described beta-1,3D-glucan extracted from baker's yeast as "a broad spectrum enhancer of host defence mechanisms stimulating humoral and cell-mediated immunity". They concluded from their research into the effects of gamma radiation on animals that "results have demonstrated the ability of glucan to influence positively the course of the acute radiation disease".[29] If a nuclear disaster were to occur, then glucan could mean the difference between life and death.

Patchen et al. state that "glucans significantly enhanced survival in otherwise lethally irradiated mice". None of the control mice survived the lethal gamma radiation, whereas the majority of mice given beta-1,3D-glucan did survive the lethal radiation.[30] Many of these studies were carried out by the US military at Bethesda, Maryland, USA.

Additionally, another radioprotective effect was discovered, whereby enhanced recovery was attributed to the free-radical scavenging ability of glucan. Myra Patchen, PhD, was the first to discover the free-radical scavenging abilities of beta-1,3D-glucan and to show that macrophages were protected from free radical attack during and after radiation, while conducting radiation experiments on animals at the Armed Forces Radiobiology Research Institute, Bethesda, Maryland, USA.[31]

Beta-1,3D-glucan has been shown to work synergistically with other radioprotective agents. Patchen et al. stated that "it was demonstrated that the postirradiation administration of glucan, an immunomodulator and haematopoietic stimulant, enhances the radioprotective effects of WR-2721".[32]

CHOLESTEROL REDUCTION

Beta-1,3D-glucan lowers cholesterol levels. Researchers from the University of Massachusetts, USA, studied the effect of yeast-derived beta-1,3D-glucan on serum lipid levels in obese, hypercholesterolaemic men. They concluded that "yeast-derived beta-glucan fiber significantly lowered total cholesterol concentrations and was well tolerated".[33]

Clinical trials of oat-derived beta-glucan and cholesterol were conducted by researchers from the University of Göteborg,

Sweden. The found that "beta-glucan mediates an increase in bile acid excretion, which most probably explains the effect of oat fibre in lowering serum lipids".[34]

Researchers from the University of Ottawa, Canada, went further and designed a randomised clinical trial to determine whether it was the presence beta-1,3D-glucan in oat bran that was responsible for oat bran's cholesterol-lowering effect. The results of the clinical trials were quite clear, that "the main component of the soluble fibre of oats, beta-glucan, significantly reduced the total and LDL cholesterol levels of hypercholesterolaemic adults without changing HDL cholesterol".[35] This means that beta-1,3D-glucan lowered the "bad" type of cholesterol without lowering levels of the "good" cholesterol.

Lipid levels in the blood are of critical importance to those with diabetes, so researchers in Switzerland investigated the effect of beta-1,3D-glucan on diabetic patients. They concluded that "Diabetic individuals can benefit from diets that are high in beta-glucan".[36]

...the simple carbohydrate beta-1,3D-glucan can be extracted from a variety of natural sources.

Lentinan is a beta-1,3D-glucan isolated from the shiitake mushroom, *Lentinus edodes*.

WOUND HEALING

Beta-1,3D-glucan has been investigated for its effect on accelerating wound healing in animals. Researchers made identical cuts on each of the rear legs of animals. Beta-glucan was applied to one leg and a saline treatment was applied to the other leg. They wrote that "During the days when the differences were most obvious, 60% to 80% of the animals showed more advanced healing in the glucan-treated wound" and concluded that "the average time for complete wound healing was reduced by about 18% as a result of glucan treatment". Histological analysis showed that "the acceleration of wound healing was mediated by early arrival of macrophages to the wound area in the glucan-treated wounds".[37]

Further evidence of rapid wound healing was shown by Browder et al. on wounds made in rats. The authors stated that wound "breaking strength was significantly increased by intravenous glucan and topical glucan on the fourth day after incision, compared with controls".[38]

Similarly, Portera et al. state that "immunomodulators that enhance macrophage function have been shown to be beneficial in a number of wound-healing models in humans".[39]

AIDS THERAPY

As mentioned, the simple carbohydrate beta-1,3D-glucan can be extracted from a variety of natural sources. Lentinan is a beta-1,3D-glucan isolated from the shiitake mushroom, *Lentinus edodes*.

Early-stage clinical trials have been carried out at San Francisco General Hospital, USA. Gordon et al. wrote that "patients in the study have shown a trend toward increases in CD4 cells and, in some patients, neutrophil activity"; however, because of the small number of patients, these values do not have statistical significance. Yet in their conclusion they noted that "a trial of lentinan in combination with didanosine (ddI) showed a mean increase of 142 CD4 cells/mm^3 over a twelve-month period, in contrast to a decrease in CD4 cells in patients on ddI alone".[40]

According to G. Chihara from Teikyo University, Kawasaki, Japan, beta-1,3D-glucans derived from lentinan "increased host resistance to various kinds of bacterial, viral and parasitic infections including AIDS" and "are the most appropriate drugs to prevent cancer recurrence or the manifestation of AIDS symptoms in HIV carriers".[41]

Endnotes

1. Czop, J.K., Valiante, N.M. and Janusz, M.J. (Harvard Medical School, Boston, Massachusetts). Phagocytosis of particulate activators of the human alternative complement pathway through monocyte beta-glucan receptors. *Prog. Clin. Biol. Res.* 1989; 297:287-96.

2. op. cit.

3. Inai et al. Activation of the Alternative Complement Pathway by Water-Insoluble Glucans of *Streptococcus mutans*: the Relation between their Chemical Structures and Activating Potencies. *Journal of Immunology* 1976; 117:1256-1260.

4. Goldman, R. Characteristics of the B-glucan Receptor of Murine Macrophages. *Exp. Cel. Res.* 1988; 174:481-490.

5. Sakai, T., Ikegami, K., Yoshinaga, E., Uesugi-Hayakawa, R. and Wakizaka, A. Rapid, sensitive and simple detection of candida deep mycosis by amplification of 18S ribosomal RNA gene; comparison with assay of serum beta-D-glucan level in clinical samples. *Tohoku J. Exp. Med.* Feb 2000; 190(2):119-28.

6. Carrow, D.J. Beta-1,3-glucan as a Primary Immune Activator. US Patent No. 5,504,079, 1996.

7. Spiros, J. Method for immune system activation by administration of beta (1-3) glucan which is produced by *Saccharomyces v erevisiae* strain R4. *Townsend Letter for Doctors*, June 1996.

8. Morikawa, K., Takeda, M., Yamazaki, M. and Mizuno, D. Induction of tumoricidal activity of polymorphonuclear leukocytes by a linear ß-1,3-D-glucan and other immunomodulators in murine cells. *Cancer Res.* 45:1496-1501.

9. Olson, E.J., Standing, J.E., Griego-Harper, N., Hoffman, O.A. and Limper, A.H. Fungal beta-glucan interacts with vitronectin and stimulates tumor necrosis factor alpha release from macrophages. *Infect. Immun.* Sept 1996; 64(9):3548-54.

10. Yadomae, T. (Laboratory for Immunopharmacology of Microbial Products, School of Pharmacy, Tokyo University of Pharmacy and Life Science, Japan), *Yakugaku Zasshi* May 2000; 120(5):413-31.

11. Bogwald, J., Johnson, E. and Seljelid, R. The cytotoxic effect of mouse macrophages stimulated *in vitro* by a beta-1,3-D-glucan from yeast cell walls. *Scand. J. Immunol.* March 1982; 15(3):297-304.

12. Di Luzio, N.R., Williams, D.L., McNamee, R.B. and Malshet, V.G. Comparative evaluation of the tumor inhibitory and antibacterial activity of solubilized and particulate glucan. Recent Results. *Cancer Res.* 1980; 75:165-72.

13. Di Luzio, N.R., McNamee, R.B., Williams, D.L., Gilbert, K.M. and Spanjers, M.A. Induced inhibition of tumor growth and enhancement of survival in a variety of transplantable and spontaneous murine tumor models. *Adv. Exp. Med. Biol.* 1980; 121(A):269-90.

14. Aoki, T. Lentinan. Chapter 4 in *Modulation Agents and their Mechanism* (Richard L. Fenichel, ed.), Marcel Dekker, Inc., New York and Basel, 1984, pp. 63-77.

15. Seljelid, R.A. Water-soluble aminated beta-1,3D-glucan derivative causes regression

Continued on page 38

THE VITAMIN C CONNECTION

Sometimes it is useful to compare the activity of a macrophage with the activity of a motor car. In order to activate the car, one first needs the car key to switch on the car. This is analogous to the way beta-1,3D-glucan can activate the macrophage cell. In order for the car to be used a lot, it obviously needs a constant supply of fuel; so, similarly, a macrophage also needs a regular supply of fuel, especially when it is activated. This is the function of vitamin C.

It has been shown that the concentration of ascorbic acid (vitamin C) in a mature macrophage can reach 1,000 times the concentration of ascorbic acid in the blood.[42] Yet it has also been shown that when macrophages are activated with beta-1,3D-glucan, they exhibit a significant drop in their vitamin C content.[43] This is because they are burning fuel.

Vitamin C is a kind of fuel that is necessary for an activated macrophage to function properly. When macrophages are not activated, then the body does not use up much vitamin C; but once macrophages are activated, the body uses up its supply of vitamin C at a very fast rate. It has been shown that it is the colony stimulating factor, produced by an activated macrophage, that causes our macrophages to uptake this extra vitamin C.[44] In fact, if the activated macrophage does not get an adequate supply of vitamin C, it is unable to function properly.

Studies have shown that animals fed vitamin C–deficient diets develop much fewer and smaller macrophages, and those macrophages have an impaired ability to move around the body to where they are needed.[45]

Additionally, vitamin C–deficient macrophages show a decreased ability to generate anti-cancer and bacteria-killing chemicals such as superoxide, even if they are activated.[46]

So, macrophages activated by beta-1,3D-glucan perform strongly for a short while until they use up all their available vitamin C; then, due to lack of vitamin C, their performance may be impaired.

So vitamin C supplementation would seem to be a necessary adjunct to beta-1,3D-glucan therapy.

The synergistic relationship between beta-1,3D-glucan and vitamin C is clearly demonstrated by *in vitro* studies on prostate cancer. Researchers achieved a greater than 95 per cent prostate cancer cell death by using a certain level of mushroom-derived beta-glucan. Yet they later found that by adding vitamin C, the same level of cancer cell death could be achieved using only one-eighth of the amount of beta-glucan.[47] The addition of vitamin C multiplied the effectiveness of the beta-glucan.

The addition of vitamin C multiplied the effectiveness of the beta-glucan.

There is much evidence to support the various beneficial effects of beta-1,3D-glucan. However, Western medicine is an evidence-based medicine. With so many conventional Western medicines having immunosuppressive effects, is it not time for the medical profession to look for an immune-booster which can enhance the effects of conventional medicines and improve patient outcomes?

People are looking for natural healing, and such natural healing can be stimulated through the use of the immune system enhancer, beta-1,3D-glucan. ∞

About the Author:
Peter Olson, BA, DipEd, has formal training in psychology and schoolteaching. As a result of friends and a family member developing cancer, he has spent the last six years conducting health research.

of solid tumors in mice. *Biosci. Rep.* Sept 1986; 6(9):845-851.
16. Mansell, P., Ichinose, H., Reed, R.J., Krementz., E.T., McNamee, R. and Di Luzio, N.R. Macrophage-mediated destruction of human malignant cells *in vivo*. *J. Natl Cancer Inst.* Mar 1975; 54(3):571-80.
17. Vetvicka, V., Thornton, B.P., Wieman, T.J. and Ross, G.D. Targeting of natural killer cells to mammary carcinoma via naturally occurring tumor cell-bound iC3b and beta-glucan-primed CR3 (CD11b/CD18). *J. Immunology* 15 July 1997; 159(2):599-605.
18. Gomaa, K., Kraus, J., Rosskopf, F., Röper, H. and Franz, G. Antitumour and immunological activity of a beta 1-3/1-6 glucan from *Glomerella cingulata*. *J. Cancer Res. Clin. Oncol.* 1992; 118(2):136-40.
19. See http://www.edenet.com/dictionary.asp.
20. Babineau, T.J., Marcello, P., Swails, W., Kenler, A., Bistrian, B. and Forse, R.A. (Harvard Medical School, Boston, Massachusetts). Randomized phase I/II trial of a macrophage-specific immunomodulator (PGG-glucan) in high-risk surgical patients. *Ann. Surg.* Nov 1994; 220(5):601-9.
21. Babineau, T.J., Hackford, A., Kenler, A., Bistrian, B., Forse, R.A., Fairchild, P.G., Heard, S., Keroack, M., Caushaj, P. and Benotti, P. (Harvard Medical School, Boston, Massachusetts). A phase II multicenter, double-blind, randomized, placebo-controlled study of three dosages of an immunomodulator (PGG-glucan) in high-risk surgical patients. *Arch. Surg.* Nov 1994; 129(11):1204-10.
22. Dellinger, E.P., Babineau, T.J., Bleicher, P., Kaiser, A.B., Seibert, G.B., Postier, R.G., Vogel, S.B., Norman, J., Kaufman, D., Galandiuk, S. and Condon, R.E. (University of Washington School of Medicine). Effect of PGG-glucan on the rate of serious postoperative infection or death observed after high-risk gastrointestinal operations. *Arch. Surg.* Sept 1999; 134(9):977-83.
23. De Felippe, Jr, J., da Rocha e Silva, Jr, M., Maciel, F.M., Soares, A. de M. and Mendes, N.F. (Hospital Arthur Ribeiro de Saboya, São Paulo, Brazil). Infection prevention in patients with severe multiple trauma with the immunomodulator beta 1-3-polyglucose (glucan). *Surg. Gynecol. Obstet.* Oct 1993; 177(4):383-8.
24. Browder, W., Williams, D., Pretus, H., Olivero, G., Enrichens, F., Mao, P. and Franchello, A. (Tulane University, New Orleans, USA). Beneficial effect of enhanced macrophage function in the trauma patient. *Ann. Surg.* May 1990; 211(5):605-12, discussion 612-3.
25. Thornton, B.P., Vetvicka, V. and Ross, G.D. Natural antibody and complement-mediated antigen processing and presentation by B-lymphocytes. *J. Immunology* 1994; 152:1727-1737.
26. Williams, D.L. and Di Luzio, N.R. Glucan-induced modification of murine viral hepatitis. *Science* 4 April 1980; 208(4439):67-9.
27. Patchen, M.L., MacVittie, T.J. and Weiss, J.F. Combined modality radioprotection: the use of glucan and selenium with WR-2721. *Int. J. Radiat. Oncol. Biol. Phys.* May 1990; 18(5):1069-75.
28. Patchen, M.L., MacVittie, T.J. and Jackson, W.E. Postirradiation glucan administration enhances the radioprotective effects of WR-2721. *Radiat. Res.* Jan 1989; 117(1):59-69.

Continued on page 83

The Medical Benefits of Beta-1,3D-Glucan

Continued from page 38

29. Hofer, M. and Pospisil, M. Glucan as stimulator of hematopoiesis in normal and gamma-irradiated mice. *Int. J. of Immunopharmacology* Sept-Oct 1997; 19(9-10):607-9.
30. Patchen, M.L. and MacVittie, T.J. Comparative effects of soluble and particulate glucans on survival in irradiated mice. *J. Biol. Response Mod.* Feb 1986; 5(1):45-60.
31. Patchen, M.L., D'Alesandro, M.M., Brook, I., Blakely, W.F. and MacVittie, T.J. Glucan: mechanisms involved in its "radioprotective" effect. *J. Leukoc. Biol.* Aug 1987; 42(2):95-105.
32. Patchen, MacVittie and Jackson, op. cit. (see endnote 28).
33. Nicolosi, R., Bell, S.J., Bistrian, B.R., Greenberg, I., Forse, R.A. and Blackburn, G.L. (University of Massachusetts, Lowell, USA). Plasma lipid changes after supplementation with beta-glucan fiber from yeast. *Am. J. Clin. Nutr*. Aug 1999; 70(2):208-12.
34. Lia, A., Hallmans, G., Sandberg, A.S., Sundberg, B., Aman, P. and Andersson, H. (University of Göteborg, Sweden). Oat beta-glucan increases bile acid excretion and a fiber-rich barley fraction increases cholesterol excretion in ileostomy subjects. *Am. J. Clin. Nutr.* Dec 1995; 62(6):1245-51.
35. Braaten, J.T., Wood, P.J., Scott, F.W., Wolynetz, M.S., Lowe, M.K., Bradley-White, P. and Collins, M.W. (University of Ottawa, Canada). Oat beta-glucan reduces blood cholesterol concentration in hypercholesterolaemic subjects. *Eur. J. Clin. Nutr*. July 1994; 48(7):465-74.
36. Wursch, P. and Pi-Sunyer, F.X. (Nestlé Research Centre, Lausanne, Switzerland). The role of viscous soluble fibre in the metabolic control of diabetes. A review with special emphasis on cereals rich in beta-glucan. *Diabetes Care* November 1997; 20(11):1774-80.
37. Wolk, M. and Danon, D. Promotion of wound healing by yeast glucan evaluated on single animals. *Med. Biol.* 1985; 63(2):73-80.
38. Browder, W., Williams, D., Lucore, P., Pretus, H., Jones, E. and McNamee, R. (Department of Surgery, Tulane University School of Medicine, New Orleans, LA, USA). Effect of enhanced macrophage function on early wound healing. *Surgery* Aug 1988; 104(2):224-30.
39. Portera, C.A., Love, E.J., Memore, L., Zhang, L., Muller, A., Browder, W. and Williams, D.W. (Department of Surgery, East Tennessee State University, TN, USA). Effect of macrophage stimulation on collagen biosynthesis in the healing wound. *Am. Surg.* Feb 1997; 63(2):125-31.
40. Gordon, M., Bihari, B., Goosby, E., Gorter, R., Greco, M., Guralnik, M., Mimura, T., Rudinicki, V., Wong, R. and Kaneko, Y. (AIDS Activities Division, San Francisco General Hospital, CA, USA). A placebo-controlled trial of the immune modulator, lentinan, in HIV-positive patients: a phase 0 - I/II trial. *J. Med.* 1998; 29(5-6):305-30.
41. Chihara, G. (Teikyo University, Kawasaki, Japan). Recent progress in immunopharmacology and therapeutic effects of polysaccharides. *Dev. Biol. Stand.* 1992; 77:191-7.
42. Vera, J.C., Rivas, C.I. and Zhang, R.H. Colony stimulating factors signal for increased transport of vitamin C in human host defense cells. *Blood* 1 April 1998; 91(7):2536-46.
43. Ber, Leonid, MD. Yeast Derived Beta-1,3-D-Glucan: An Adjuvant Concept. *American Journal of Natural Medicine* Nov 1997; 4(9).
44. Vera, Rivas and Zhang, op. cit. .
45. Ganguly, R., Durieux, M.F. and Waldman, R.H. Macrophage function in vitamin C–deficient guinea pigs. *Am. J. Clinical Nutrition* July 1976; 29(7):762-5.
46. Ganguly, R. and Waldman, R.H. Macrophage functions in aging: effects of vitamin C deficiency. *Allergic Immunol.* (Leipz.) 1985; 31(1)37-43.
47. Fullerton, S.A., Samadi, A.A., Tortorelis, D.G., Choudhury, M.S., Mallouh, C. and Tazaki, H. Induction of apoptosis in human prostatic cancer cells with beta-glucan. *Mol. Urol.* Spring 2000; 4(1):7-14.